Amendments to the Claims

The current status of all claims is listed below and supercedes all previous lists of claims.

Please cancel claims 1-101 without prejudice to the applicants' right to reinstate those claims or pursue the subject matter of the cancelled claims in a further application.

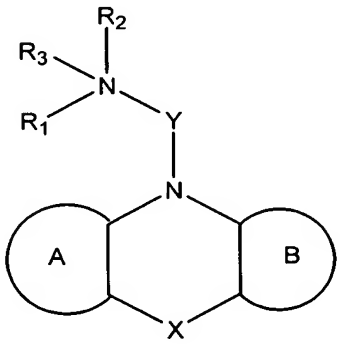
1-101. (Cancelled)

Please add claims 102-174 as follows.

102 (New). A method of treating a patient with a *M. tuberculosis* infection comprising administering to the patient an amount of a composition comprising an electron transport chain inhibitor, wherein said amount is effective to inhibit the electron transport chain in said *M. tuberculosis* does not have anti-dopaminergic effects in said patient.

103 (New). The method of claim 102 wherein said inhibitor is an oligonucleotide, a small molecule, a mimetic, a decoy, or an antibody.

104 (New). The method of claim 102 wherein said inhibitor is a small molecule of formula I,



I

wherein:

A and B are each independently aryl or heteroaryl and each are optionally substituted with 1-3 substituents selected from the group consisting of halogen, CHO, COR_4, C_1-C_6

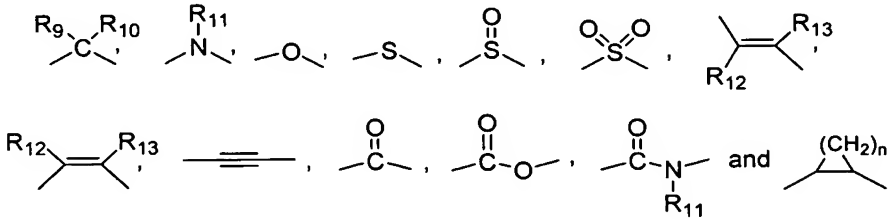
alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_1-C_6 alkenyl, C_1-C_6 alkynyl, C_1-C_6 alkoxy, phenyl (optionally substituted with 1-3 substituents selected from halogen, C_1-C_3 alkyl, C_1-C_3 haloalkyl, C_1-C_3 alkoxy, cyano, nitro, COOH, and CO_2R_4), heteroaryl (optionally substituted with 1-3 substituents selected from halogen, C_1-C_3 alkyl, C_1-C_3 haloalkyl, C_1-C_3 alkoxy, cyano, nitro, COOH, CO_2R_4), cyano, nitro, C_1-C_6 thioalkyl, C_1-C_6 thiohaloalkyl, C_1-C_6 alkylthiol, $(CH_2)_nCOOH$, $(CH_2)_nCO_2R_4$, $(CH_2)_nNR_5R_6$, $(CH_2)_nCONR_5R_6$, OH, SH, $(CH_2)_nNR_7COR_8$, $(CH_2)_nSOR_4$, SO_2R_4, $(CH_2)_nSONR_5R_6$, and $(CH_2)_nSO_2NR_5R_6$; and

n is an integer, wherein each n is independently selected from 0 to 6; and

R_4-R_8 are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, and phenyl (optionally substituted with from 1-3 substituents selected from halogen, C_1-C_3 alkyl, C_1-C_3 haloalkyl, C_1-C_3 alkoxy, cyano, nitro, COOH, CO_2Me); or

R_5 and R_6 together with the nitrogen they are attached form a 5 to 7 member ring; and

Y is a linker unit consisting of 1 to 6 atoms or atom groups wherein the atom or atom groups are selected from the following:



and R_9 through R_{13} are each independently selected from a group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, and phenyl (optionally substituted with from 1-3 substituents selected from halogen, C_1-C_3 alkyl, C_1-C_3 haloalkyl, C_1-C_3 alkoxy, cyano, nitro, COOH, CO_2Me); and

R_1 and R_2 are each independently hydrogen, C_1-C_6 alkyl, $(CH_2)_nNR_4R_5$, phenyl (optionally substituted with 1-3 substituents selected from halogen, C_1-C_3 alkyl, C_1-C_3 haloalkyl, C_1-C_3 alkoxy, cyano, nitro, COOH, CO_2Me), CO_2R_4, $CO_2(CH_2)_n$phenyl (optionally substituted with from 1-3 substituents selected from halogen, C_1-C_3 alkyl, C_1-C_3 haloalkyl, C_1-C_3 alkoxy, cyano, nitro, COOH, CO_2Me), C_1-C_6 haloalkyl, cycloalkyl (optionally substituted with from 1-3 substituents selected from NR_5R_6, halogen, and C_1-C_6 alkyl),

heterocycloalkyl including 1-3 hetero ring atoms selected from NR_{11}, O and S, optionally substituted with 1-3 substituents selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 hydroxyalkyl, C_1-C_6 haloalkyl, NO_2, CN, and $(CH_2)_nNR_4R_5$ or

R_1 and Y together with the nitrogen that they are attached form a 3 to 7 member ring; or

R_1 or R_2 together with the nitrogen that they are attached form a 3-7 member ring optionally containing from 1 to 3 additional heteroatoms selected from the group consisting of NR_{14}, O, and S, and optionally substituted with 1-3 substituents selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 haloalkyl, NO_2, CN, and $(CH_2)_nNR_4R_5$; and

R_{14} is C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, SO_2R_4, $SO_2NR_5R_6$, $CO(CH_2)_n$phenyl (optionally substituted with 1-3 substituents selected from C_1-C_6 alkyl, NR_5R_6, NO_2), $(CH_2)_n$phenyl (optionally substituted with 1-3 substituents selected from C_1-C_6 alkyl, halogen, NH_2, OH, OR, NO_2), CO_2R_4; and

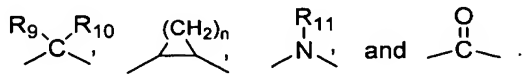
X is NR_{11}, O, S, SO, or SO_2; and

when both R_1 and R_2 are not hydrogen, R_3 is optionally present as H, C_1-C_6 alkyl, $(CH_2)_n$phenyl (optionally substituted with 1-3 groups selected from the group consisting of C_1-C_6 alkyl, halogen, NO_2, cyano, COOH, CO_2Me), or C_1-C_6 haloalkyl.

105 (New). A method according to claim 104, wherein for the compound of formula I:

A and B are each aryl independently and optionally substituted with 1-3 substituents selected from the group consisting of halogen, C_1-C_3 haloalkyl, C_1-C_3 thioalkyl, C_1-C_3 thiohaloalkyl, cyano, $SO_2NR_5R_6$, SO_2R_4 and C_1-C_6 alkoxy; and

Y is a linker unit consisting of 1 to 4 atoms or atom groups wherein the atom or atom group is selected from the following



106 (New). A method according to claim 105 wherein each aryl is independently naphthyl or phenyl.

107 (New). A method according to claim 105 wherein A and B are each phenyl and each phenyl is independently and optionally substituted with one substituent selected from halogen, CF_3, SMe, SCF_3, cyano, $SO_2N(Me)_2$, OMe, and SO_2Me; and X is S or SO_2.

108 (New). A method according to claim 107 wherein A is unsubstituted and B is substituted with Cl at the position para to X.

109 (New). A method according to claim 107 wherein A is unsubstituted and B is substituted with CF_3 at the position para to X.

110 (New). A method according to claim 107 wherein A is unsubstituted and B is substituted with SMe at the position para to X.

111 (New). A method according to claim 107 wherein A is unsubstituted and B is substituted with SCF_3 at the position para to X.

112 (New). A method according to claim 107 wherein A is unsubstituted and B is substituted with $SO_2N(Me)_2$ at the position para to X.

113 (New). A method according to claim 107 wherein A is unsubstituted and B is substituted with OMe at the position para to X.

114 (New). A method according to claim 107 wherein A is unsubstituted and B is substituted with cyano at the position para to X.

115 (New). A method according to claim 107 wherein A is unsubstituted and B is substituted with SO_2Me at the position para to X.

116 (New). A method according to claim 107 wherein Y is $(CH_2)_3$; and R_1 and R_2 together form a 6-member ring with NR_{11} at the 4-position of the 6-member ring.

117 (New). A method according to claim 107 wherein Y is $(CH_2)_3$; and R_1, R_2 and R_3 are each methyl.

118 (New). A method according to claim 107 wherein Y is $(CH_2)_3$; and R_1 is benzyl, R_2 is methyl and R_3 is methyl.

119 (New). A method of treating a patient with a *M. tuberculosis* infection comprising administering to the patient an amount of a composition comprising a first inhibitor in combination with a second inhibitor, wherein said first inhibitor is administered in amounts effective to inhibit an electron transport system in said *M. tuberculosis* but wherein said amount is not effective as an anti-dopaminergic in said patient, and wherein said second inhibitor is a traditional anti-tuberculosis medicament.

120 (New). The method of claim 119 wherein the second inhibitor is isoniazid, rifampin, streptomycin, pyrazinamide or ethambutol.

121 (New). The method of claim 119 wherein said first and second inhibitors each has an IC50 greater than 300 μM in a D2 dopamine receptor binding assay.

122 (New). The method of claim 119 wherein said first and second inhibitors each has an IC50 less than 30 μM in an electron transport system model.

123 (New). The method of claim 119 wherein said first and second inhibitors each has an IC50 less than 30 μM in an electron transport system model and an IC50 greater than 100 μM in a D2 dopamine receptor binding assay.

124 (New). A method of modulating Type II NADH dehydrogenase in *M. tuberculosis* comprising contacting said cell with an amount of a composition comprising a *M. tuberculosis* modulator, said amount effective to inhibit an electron transport chain in said *M. tuberculosis* by at least 50%.

125 (New). A method of protecting an animal from a *M. tuberculosis* infection comprising administering to said animal an amount of a composition comprising a *M. tuberculosis* electron transport chain polypeptide modulator effective to inhibit the electron transport chain in *M. tuberculosis.*

126 (New). The method of claim 102 wherein inhibition of the electron transport chain is detected by measuring one or more of: oxidation of NADH, growth inhibition of *M. tuberculosis* or *M. smegmatis*, inhibition of respiration of *M. tuberculosis* or *M. smegmatis*, or inhibition of replication of *M. tuberculosis* or *M. smegmatis.*

127 (New). The method of claim 126 wherein inhibition is at least 50% as compared to a control.

128 (New). The method of claim 102 wherein the electron transport chain is inhibited by inhibiting one or more type II NADH dehydrogenase, menaquinone, flavin adenine dinucleotide, bc1 complex, cytochrome bd oxidase, fumarate reductase, or nitrate reductase.

129 (New). The method of claim 128 wherein the type II NADH dehydrogenase is type II NADH dehydrogenase *ndh* or type II NADH dehydrogenase *ndhA*.

130 (New). The method of claim 102 wherein said effective amount inhibits the electron transport system in *M. tuberculosis* and does not have extrapyramidal side effects in said patient.

131 (New). The method of claim 102 wherein said effective amount inhibits the electron transport system in *M. tuberculosis* and does not block dopamine receptors.

132 (New). The method of claim 102 wherein said inhibitor exhibits reduced side effects compared to treatment with a composition having anti-dopaminergic effects.

133 (New). The method of claim 102 wherein the patient has not been diagnosed as having one or more psychological diseases or disorders at the time of treatment.

134 (New). The method of claim 102 wherein the patient is not classified as psychotic according to the criteria of DSM-IV.

135. (New). The method of claim 102 wherein said composition is effective at a concentration of less than about 10 μM to inhibit electron flow by at least 50% in an *in vitro* assay of electron transport.

136 (New). The method of claim 102 wherein said inhibitor is an antibody selective for a *M. tuberculosis* electron transport chain polypeptide.

137 (New). The method of claim 136 wherein said *M. tuberculosis* electron transport chain polypeptide has an amino acid sequence of SEQ ID NO:1, 3, 5, 7, 9 or 11.

138 (New). The method of claim 102 wherein said *M. tuberculosis* is resistant to one or more of isoniazid, rifampin, streptomycin, pyrazinamide and ethambutol.

139 (New). The method of claim 130 wherein said side-effects are selected from the group consisting of Dystonia, drooling, tremors, Tardive diskensia, Neuroleptic Malignant

Syndrome (NMS), hyperpyrexia, muscle rigidity, altered mental status, autonomic instability (irregular pulse, abnormal blood pressure, tachycardia, disphoresis), anemia, jaundice, diminishing the effect of oral anti-coagulants, causes chromosomal aberrations in rodents, drowsiness, dizziness, skin reaction, rash, dry mouth, insomnia, amenorrhea, fatigue, muscle weakness, anorexia, lactation, blurred vision, motor restlessness, spasms, and neuromuscular reaction.

140 (New). The method of claim 102 wherein the inhibitor is an antisense oligonucleotide comprising at least 80% sequence homology to the complement of a nucleic acid molecule encoding a *M. tuberculosis* electron transport chain polypeptide (SEQ ID NO:2, 4, 6, 8, 10 or 12), wherein said antisense oligonucleotide specifically hybridizes to the nucleic acid molecule and inhibits *M. tuberculosis* electron transport chain polypeptide mRNA levels by at least 50% in *M. tuberculosis*.

141 (New). The method of claim 140 wherein said antisense oligonucleotide specifically hybridizes with the 5' UTR, start codon region, intron/exon region, coding region, stop codon region, or 3'UTR of said polynucleotide.

142 (New). The method of claim 102 wherein the antisense oligonucleotide comprises at least 95% sequence homology to the complement of a nucleic acid molecule encoding *M. tuberculosis* electron transport chain polypeptide (SEQ ID NO:2, 4, 6, 8, 10 or 12).

143 (New). The method of claim 102 wherein said inhibitor is an antisense oligonucleotide specifically hybridizable to an electron transport chain polynucleotide, wherein said electron transport chain polynucleotide is type II NADH dehydrogenase, menaquinone, flavin adenine dinucleotide, bc1 complex, cytochrome bd oxidase, fumarate reductase, or nitrate reductase.

144 (New). The method of claim 140 wherein said antisense oligonucleotide inhibits *M. tuberculosis* electron transport chain polypeptide mRNA levels by at least 90% in *M. tuberculosis*.

145 (New). The method of claim 102 further comprising administering to said patient a composition comprising one or more of isoniazid, rifampin, streptomycin, pyrazinamide or ethambutol.

146 (New). The method of claim 102 wherein said inhibitor has an IC50 greater than 300 μM in a D2 dopamine receptor binding assay.

147 (New). The method of claim 102 wherein said inhibitor has an IC50 less than 10 μM in an electron transport system model.

148 (New). An isolated polypeptide comprising an electron transport chain polypeptide comprising a sequence of SEQ ID NO: 1, 3, 5, 7, 9 or 11, or a fragment thereof, said fragment comprising at least 10 amino acid residues, and said fragment comprising at least one epitope of the electron transport chain polypeptide.

149 (New). The polypeptide of claim 148 wherein said electron transport chain polypeptide is an *M. tuberculosis* or *M. smegmatis* electron transport chain polypeptide.

150 (New). The polypeptide of claim 148 wherein said polypeptide binds specifically to an anti-type II NADH dehydrogenase antibody.

151 (New). An isolated epitope-bearing fragment of a polypeptide comprising a sequence of SEQ ID NO: 1, 3, 5, 7, 9 or 11, said fragment comprising between about 6 and about 20 contiguous amino acids of SEQ ID NO: 1, 3, 5, 7, 9 or 11.

152 (New). An isolated anti-electron transport chain polypeptide antibody obtained by immunization of a subject with the epitope-bearing fragment of claim 151.

153 (New). An isolated antibody which specifically recognizes at least one region of a polypeptide comprising a sequence of SEQ ID NO: 1, 3, 5, 7, 9 or 11.

154 (New). The isolated antibody of claim 153, wherein said antibody binds to a catalytic, hydrolytic or binding region of the polypeptide.

155 (New). The isolated antibody of claim 153 wherein said polypeptide is an *M. tuberculosis* or *M. smegmatis* electron transport chain polypeptide.

156 (New). The isolated antibody of claim 153 wherein said antibody is selected from the group consisting of a monoclonal antibody, a polyclonal antibody, a chimeric antibody, a humanized antibody, a single-chain antibody or a Fab fragment.

157 (New). The isolated antibody of claim 153 wherein said antibody is labeled.

158 (New). The isolated antibody of claim 157 wherein said label is an enzyme, radioisotope, or fluorophore.

159 (New). The antibody of claim 153 wherein the binding affinity of said antibody is less than about 1 x 10^5 K_a for a polypeptide other than an electron transport chain polypeptide.

160 (New). An isolated cell that produces the antibody of claim 153.

161 (New). A hybridoma that produces the antibody of claim 153.

162 (New). A composition comprising the anti-electron transport chain polypeptide antibody of claim 153 and a pharmaceutically acceptable carrier.

163 (New). A method of treating a tuberculosis patient comprising administering to said patient a therapeutically effective amount of the antibody of claim 153.

164 (New). An immunogenic composition comprising a polynucleotide encoding a *M. tuberculosis* electron transport chain polypeptide having at least 90% sequence homology to SEQ ID NO:1, 3, 5, 7, 9 or 11, or immunogenic fragment thereof, said fragment having at least 10 amino acid residues.

165 (New). The immunogenic composition of claim 164 wherein said polynucleotide has the amino acid sequence of SEQ ID NO:2, 4, 6, 8, 10 or 12.

166 (New). A composition comprising a recombinant vaccine comprising a nucleotide sequence that encodes a *M. tuberculosis* electron transport chain polypeptide having the amino acid sequence of SEQ ID NO:1, 3, 5, 7, 9 or 11, or immunogenic fragment thereof having at least 10 amino acid residues, operably linked to regulatory elements.

167 (New). A composition comprising a live attenuated pathogen comprising a nucleotide sequence that encodes one or more *M. tuberculosis* electron transport chain polypeptides or functional fragments thereof, said fragments having at least 10 amino acid residues.

168 (New). An injectable pharmaceutical composition comprising the composition of claim 164.

169 (New). A pharmaceutical dosage form comprising the composition of claim 164, wherein said pharmaceutical dosage form is a solid dosage form selected from the group

consisting of tablets, caplets, beads, or capsules, or a liquid dosage form selected from the group consisting of a syrup, elixir, solutions or suspension.

170 (New). A method of immunizing an individual against *M. tuberculosis* comprising administering to said individual the composition of claim 167.

171 (New). A method of inducing an immune response in an individual against *M. tuberculosis* comprising administering to said individual the composition of claim 166.

172 (New). The method of claim 102 wherein the *M. tuberculosis* is in a dormant state.

173 (New). A method for detecting the presence of *M. tuberculosis* in a sample comprising: contacting the sample with an electron transport chain inhibitor comprising a detectable label and detecting evidence of the electron transport chain inhibitor in said sample, wherein evidence of the electron transport chain inhibitor is indicative of the presence of *M. tuberculosis*.

174 (New). The method of claim 173 wherein said sample is a human sample.